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Polybrominated diphenyl ethers in UK human milk; Implications for infantile exposure and relationship to external exposure

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Abstract

Fourteen tri-deca polybrominated diphenyl ethers (PBDEs) were investigated in 35 human milk samples from Birmingham, UK. While none of the hepta-nona BDEs (the main components of the OctaBDE technical mixture) were above the limit of quantitation (LOQ); BDE-47 (average concentration = 3.3 ng g^{-1} lipid weight (lw)) was quantified in all samples contributing 34-74% to Σtri-hexa BDEs (the principal constituents of the PentaBDE commercial formulation). BDE-209 (the main congener in the DecaBDE formulation) was present above the LOQ in 69% of samples (average concentration = 0.31 ng g^{-1} lw). Concentrations of Σtri-hexa BDEs ranged from 0.2-26 ng g^{-1} lw with concentrations of BDE-47 > BDE-153> BDE-99. While concentrations of Σtri-hexa BDEs in this study (average = 5.95 ng g^{-1} lw) were at the high end of those reported from other European countries, concentrations of BDE-209 were lower than those reported in human milk from other countries. The average exposure of a UK nursing infant to Σtri-hexa BDEs (35 ng (kg bw)$^{-1}$ day^{-1}) via breast milk exceeded the upper-bound dietary intakes of both UK adults and toddlers. Using a simple one compartment pharmacokinetic model, PBDE intakes of UK adults via inhalation, diet and dust ingestion were converted to predicted body burdens. Predictions compared well with those observed for Σtri-hexa BDEs and BDE-209 in breast milk.

Keywords: PBDEs, human milk, infant exposure, BDE 209.

Introduction

Polybrominated diphenyl ethers (PBDEs) have been extensively used as flame retardants for a wide range of consumer products including furniture, carpets, mattresses and casings for electronic equipment (BSEF 2013). Three technical PBDE formulations were commercially available: Penta (consisting primarily of BDE-47 and BDE-99 – 38-49% each, alongside smaller amounts of other tri- to hepta-BDEs), Octa (a mixture of hexa- to deca-BDEs – the exact congener composition varying substantially between the two principal formulations marketed) and Deca (92-97% decabromodiphenyl ether – BDE 209 – plus nona- (principally) and octa-BDEs) (La Guardia, et al. 2006). DecaBDE has dominated worldwide production with a global market demand of 56,100 tons in 2001, compared to 7,500 and 3,790 tons for PentaBDE and OctaBDE formulations respectively (BSEF 2013). Despite their utility, the persistence and bioaccumulative characters of these compounds have resulted in increasing concern over their potential adverse effects to human health (Frederiksen, et al. 2009; Harrad, et al. 2010). Animal studies have shown PBDEs to pose potential health risks including: endocrine disruption, neurodevelopmental and behavioural outcomes, hepatic abnormality and possibly cancer (Birnbaum and Staskal 2004; Darnerud 2008; Hakk 2010; Wikoff and Birnbaum 2011). The few data available from human epidemiological studies imply effects on: male reproductive hormones (Johnson, et al. 2013; Palace, et al. 2010), semen quality (Akutsu, et al. 2008), thyroid hormone homeostasis (Turyk, et al. 2008), cryptorchidism (Crump, et al. 2010), behavioral factors in pregnant women (Buttke, et al. 2013), as well as lower birth weight and length (Chao, et al. 2007; Lignell, et al. 2013). Such evidence has contributed to complete EU bans for Penta and OctaBDE, and restrictions on the use of DecaBDE in addition to other restrictions within several jurisdictions on the manufacture and new use of the three commercial PBDE formulations across the world (Harrad, et al. 2010). Moreover, PBDEs associated with Penta and OctaBDE have been listed under the UNEP

75 Stockholm Convention on POPs, while DecaBDE is currently under consideration for listing
76 under Annexes A, B and/or C to the convention (Stockholm convention on POPs 2009).
77 Despite such restrictions, human exposure to PBDEs is likely to continue for the foreseeable
78 future, given their persistence and ubiquity of flame-retarded consumer materials (Harrad and
79 Diamond 2006).
80 Several studies have reported different levels of PBDEs in various human tissues including
81 serum, placenta, liver, adipose tissue and breast milk from different European, Asian and
82 North American countries in the last few years (Cui, et al. 2012; Frederiksen, et al. 2009).
83 These biomonitoring data provide a direct measurement of the human body burden of BFRs
84 resulting from various external exposure pathways (e.g. inhalation, ingestion of dust, diet and
85 water) and contribute to the risk assessment of such compounds. However, the only available
86 information on BFRs in UK human samples is for tri- to hexa-BDEs (major components of
87 the PentaBDE commercial product) where the median concentrations for Σtri-to hexa-BDEs
88 in human milk and serum samples collected in 2003 were 6.3 and 4.18 ng g^{-1} lipid weight
89 (lw) respectively (Kalantzi, et al. 2004). In addition, BDE-209 was detected in 11 out of 153
90 serum samples at concentrations from 0.015-0.240 ng g^{-1} lw) (Thomas, et al. 2006).
91 Current understanding is that non-occupational human exposure to PBDEs occurs mainly via
92 a combination of diet, air and indoor dust (either via ingestion or dermal contact)
93 (Frederiksen, et al. 2009; Lorber 2008; Trudel, et al. 2011). However, the extent to which the
94 known contamination of indoor environments with PBDEs influences human body burdens
95 remains unclear. While some studies have managed to establish significant positive
96 correlations between the levels of PBDEs in food or indoor dust and their concentrations in
97 human milk or serum (Dunn, et al. 2010; Thomsen, et al. 2008; Wu, et al. 2007); such
98 correlations could not be established in other studies (Roosens, et al. 2009; Wang, et al.
99 2013). An alternative approach involved application of a simple pharmacokinetic model to

predict the body burdens of PBDEs in American adults using intake data from different exposure pathways. The predicted body burdens were then compared to the reported levels of PBDEs in human matrices and the relationship between external and internal exposure of American adults to PBDEs was discussed (Lorber 2008).

To address this paucity of UK human biomonitoring data for PBDEs, this study reports concentrations of Σtri-hexa BDEs and *for the first time* BDE-209 in 35 human milk samples from Birmingham, UK. These data are then used to estimate the dietary exposure of UK nursing infants under different exposure scenarios. Finally, a simple, one-compartment pharmacokinetic model is applied to predict the body burdens of the studied PBDEs in UK adults (using indoor air and dust levels reported elsewhere by our research group for Birmingham, UK (Abdallah and Harrad 2010; Harrad and Abdallah 2011; Harrad, et al. 2006; Harrad, et al. 2008a). The model predictions are then compared to the concentrations of target compounds measured in the analyzed human milk samples (used as indicator of adult female body burdens) for further understanding of the relationship between external and internal human exposure to PBDEs in UK adults.

Materials and Methods

Sample collection

Breast milk samples (each comprising ~50 mL) were obtained from 35 adult healthy primiparous volunteers via Birmingham Women's Hospital Milk Bank after the study protocol was approved by Warwickshire Research Ethics Committee and the R&D Department in Birmingham Women's NHS foundation trust. Informed consent was obtained from all the participants before sample collection. Samples collected in 2010 were kept in clean screw-capped glass containers and transferred from the Milk Bank to the laboratory in special ice boxes then stored at -20ºC until the time of analysis. Due to ethical regulations,

the samples were collected in a completely anonymous fashion with all participant information kept strictly confidential. For the purpose of this study, only 1 milk sample was collected from each mother during her first 6 month of lactation.

Sample extraction

Accurately weighted aliquots of the freeze-dried samples (~ 2 g) were loaded into pre-cleaneds 66 mL Accelerated Solvent Extraction (ASE 300, Dionex Inc., UK) cells containing 1.5 g florisil, 3 g alumina, 5 g anhydrous Na_2SO_4 and hydromatrix (Varian Inc., UK) to fill the void volume of the cells, spiked with 25 ng of each of ^{13}C-labelled BDE-47, BDE-99, BDE-153, BDE-183, BDE-209 as internal (surrogate) standards. The ASE cells were extracted with hexane:dichloromethane (1:9, *v/v*) at 90 ˚C and 1500 psi. The heating time was 5 minutes, static time 4 min, purge time 90 s, flush volume 50%, with three static cycles. The lipid weight of the studied samples was determined gravimetrically on separate aliquots using a standard procedure (The European Standard EN 1528-2, 1996; see supplementary data for more details).

Sample Clean-up

The crude extracts were concentrated to 0.5 mL using a Zymark Turbovap® II (Hopkinton, MA, USA) then washed with 3 mL of 98% sulfuric acid. After phase separation, the hexane layer was transferred onto a florisil column topped with sodium sulfate and eluted with 25 mL of hexane:dichloromethane (1:1, v/v). The eluate was evaporated to dryness under a gentle stream of N_2 and the dried extract reconstituted in 200 µL of ^{13}C-BDE-100 (25 pg µL^{-1} in methanol) used as recovery determination (or syringe) standard to determine the recoveries of internal standards for QA/QC purposes.

147

148 *LC-APPI-MS/MS analysis*

149 Sample analysis was carried out using an LC-MS/MS system composed of a dual pump
150 Shimadzu LC-20AB Prominence liquid chromatograph equipped with SIL-20A autosampler,
151 a DGU-20A3 vacuum degasser coupled to a Sciex API 2000 triple quadrupole mass
152 spectrometer. Details of the multi-residue analytical methodology used for separation and
153 quantification of the studied PBDEs can be found elsewhere (Abdallah, et al. 2009). (A brief
154 description is given in the supplementary data section).

155

156 *Comparison of PBDE intake to human body burdens.*

157 We have previously estimated UK adult intake of the target PBDEs via inhalation, dust
158 ingestion and diet (Harrad and Abdallah 2011; Harrad, et al. 2006; Harrad, et al. 2008a;
159 Harrad, et al. 2008b) (A summary of the assumptions on which these estimations are based is
160 provided as supplementary data). To examine the relationship between these estimated
161 intakes and the body burdens indicated via human milk samples, a simple one-compartment,
162 first order pharmacokinetic (PK) model was used. The studied PBDEs were hypothesized to
163 accumulate in lipids (the single compartment in the model). Therefore, the change in PBDE
164 lipid concentration over time can be expressed by equation 1 (Lorber 2008).

165
$$\frac{\delta C_{PBDE}}{\delta t} = \frac{I_{PBDE}(t)\, x\, AF_{PBDE}}{BL(t) - K_{PBDE}\, x\, C_{PBDE}(t)} \qquad (1)$$

166 Where C_{PBDE} is the compound specific concentration in lipids (ng g^{-1} lw); I_{PBDE} is the daily
167 intake of the target BFR (ng day^{-1}); AF_{PBDE} is the absorption fraction (unitless); BL is body
168 lipid mass (g) and K_{PBDE} is the compound specific first order dissipation rate (day^{-1}).

If K_{PBDE} is assumed to be constant over time then equation 1 can be solved into:

$$C_{PBDE}(t) = C_{PBDE}(0)\ x\ e^{(-K_{PBDE}\cdot t)} + [\frac{(I_{PBDE}(t)\ x\ AF_{PBDE})}{BL(t)}]\ x\ [\frac{(1-e^{(-K_{PBDE}\cdot t)})}{K_{PBDE}}] \quad (2)$$

Where $C_{PBDE}(0)$ is the studied PBDE body lipid concentration at time 0 (initial concentration before intake).

Assuming a constant dose over time at constant body lipid mass, the steady state PBDE lipid concentration can be calculated from equation 3. It is stressed that the assumption of steady state conditions is an inherent uncertainty with this approach.

$$C_{PBDE} = \frac{(I_{PBDE}\ x\ AF_{PBDE})}{BL\ x\ K_{PBDE}} \quad (3)$$

Quality assurance/Quality control

Good recoveries (68-106%) of the ^{13}C-labelled internal standards were obtained for all the studied compounds (table SI-4). Further evaluation of the method extraction/clean up performance was achieved via spiking milk samples (n=6) with ^{13}C-BDE-154 prior to freeze drying and excellent recoveries (>90%) were obtained (table SI-5).

No target compounds were detected in method blanks (n=5; consisting of 2 g pre-extracted anhydrous sodium sulfate treated exactly as a sample) or field blanks (n=5; consisting of ~2 g of broken pieces of the glass milk containers treated exactly as a sample). Therefore, there was no need for blank correction of concentrations and method limits of detection (LOD) and quantification (LOQ) were estimated based on 3:1 and 10:1 S:N ratios respectively.

The accuracy and precision of the analytical method applied for PBDE determination was assessed via replicate analysis (n=10) of NIST SRM 2585. The results obtained compared favourably with the reported reference values (table SI-6a).

Results and discussion

Concentrations of Σtri-hexa *BDEs in UK human milk*

While none of the investigated hepta- to nona-BDE congeners were above LOQ, BDE-47 was quantified in all the analysed samples contributing 34-74% to Σtri-hexa BDEs (Table 1). The predominant BDE congeners in the studied human milk were in the order BDE-47 > BDE-153> BDE-99. These 3 congeners constituted an average of 85% of the quantified Σtri-hexa BDEs in the studied samples. This is in agreement with previous reports of PBDEs in human milk from various countries (Frederiksen, et al. 2009). Interestingly, a higher average level of BDE-153 (1100 pg g^{-1} lw) than that of BDE-99 (710 pg g^{-1} lw) was observed (Table 1). While this differs from the relative contribution of these 2 PBDE congeners in the commercial PentaBDE formulations (La Guardia, et al. 2006), several authors have reported higher levels of BDE-153 than BDE-99 in human milk (Ben Hassine, et al. 2012; Dunn, et al. 2010; Frederiksen, et al. 2009). In addition, a recent study has reported BDE-153 as the dominant congener in 5 human breast milk samples from California (Park, et al. 2011). Furthermore, a study of PBDEs in human milk from the Faroe islands also reported predominance of BDE-153 (Fangstrom, et al. 2005). However, such high levels of BDE-153 could not be associated with high consumption of seafood diet in the studied population, indicating that dietary exposure was not the reason for the elevated BDE-153 concentrations in breast milk. Therefore, we hypothesize that the relatively higher contribution of BDE-153 to Σtri-hexa BDEs in human milk samples than expected from the PentaBDE technical mixture may be attributed to 2 main factors:

First, the high bioaccumulation potential of BDE-153 in lipids (as evidenced by a half-life of 6.5 years compared to 1.8 and 2.9 years for BDE-47 and BDE-99 respectively (Geyer, et al. 2004)) which indicates that over time, BDE-153 will become the predominant congener in the body.

Second, the possible production of BDE-153 as a result of BDE-209 metabolic stepwise meta-meta debromination (Roberts, et al. 2011). This stepwise debromination was previously observed in peregrine falcon eggs from California, where BDE-153 was the dominant congener only in eggs with high levels of BDE-209 (Holden, et al. 2009). Interestingly, while concentrations of BDE-153 in this study were significantly ($r = 0.443$; $p<0.01$) correlated with those of BDE-209, no other statistically significant ($p<0.05$) correlation was observed between BDE-209 levels and any of the PBDE congeners or Σtri-hexa BDEs in the analyzed samples. This further supports the hypothesis that metabolic degradation of BDE-209 yields the highly bioaccumulative BDE-153 resulting in elevated concentrations of the latter in human milk.

While the levels of Σtri-hexa BDEs in this study (Table 1) are slightly lower than those reported in UK human milk samples collected in 2003 (n=54, average = 6.3 ng g^{-1} lw), these concentrations are still at the high end of those reported from other European, Asian, African and Australasian countries (Table 2). On the other hand, Σtri-hexa BDEs in UK human milk are substantially lower than those reported from USA and Canada (Table 2) which is in agreement with the far more extensive production and use of the PentaBDE technical formulation in North America than elsewhere (BSEF 2013).

Concentrations of BDE-209 in UK human milk

BDE-209 was above LOQ in 69% of the studied milk samples ranging from <0.06-0.92 ng g^{-1} lw (Table 1). To the authors' knowledge, this paper is the first to report concentrations of

BDE-209 in UK human milk. Interestingly, these levels are at the lower end of BDE-209 concentrations reported in human milk from other European countries (Table 2) despite the substantially higher levels of this BFR reported in UK indoor dust compared to the rest of Europe (Harrad, et al. 2010) and the reported higher usage of BDE 209 in the UK than other EU countries (EU Risk Assessment Report 2002). This may indicate that while indoor dust ingestion is the major pathway of external human exposure to BDE-209 (Harrad, et al. 2008a; Lorber 2008), the high levels of this compound in indoor dust do not significantly contribute to human body burdens. Our research group have recently reported on the very low bioaccessibility (~14%) of BDE-209 in indoor dust across the human gastrointestinal tract (GIT) following oral ingestion (Abdallah, et al. 2012), consistent with animal studies reporting low bioavailability (4-26%) of BDE-209 (Huwe and Smith 2007; Sandholm, et al. 2003). Such poor uptake of BDE-209 from the GIT, combined with its very short human half-life ($t_{0.5}$ = 7 days, (Geyer, et al. 2004) and its preferential partitioning to serum rather than milk fat (Mannetje, et al. 2012) may result in the apparently low influence of BDE-209 concentrations in indoor dust on UK adult body burdens.

Nursing infants' dietary intake of PBDEs via breast milk:

Breast milk is a recognized medium for direct transfer of POPs to nursing infants. To estimate the nursing infants' dietary intake of the studied BFRs via breast milk, equation 4 was used.

$$Di = \frac{C_{PBDE} \; x \, F_{lipid}}{Bw} \ldots\ldots\ldots\ldots (4)$$

Where *Di* is the estimated dietary intake (ng kg^{-1} bw day^{-1}); C_{PBDE} is the concentration of target PBDE in milk (ng g^{-1} lw); F_{lipid} is the daily lipid intake via breast milk (g day^{-1}) and *Bw* is the body weight (4.14 kg) (U.S. EPA 2002.). The infant's daily lipid intake via breast milk

(F_{lipid}) was calculated based using U.S. EPA guidelines (U.S. EPA 2002.) which suggest an average intake of 702 mL milk per day for a 1 month old infant weighing 4.14 kg. The median lipid content of the analyzed milk samples was 3.47 g lipid per 100 mL of breast milk resulting in a daily lipid intake of 24.4 g lipid day^{-1}.

Table 3 shows the estimated dietary intake of target PBDEs via breast milk using different exposure scenarios (in which exposure factors (e.g. dust ingestion rate) were held constant but using different PBDE concentrations (e.g. 25^{th} percentile) derived from our breast milk data). While the estimated average UK infant exposure to Σtri-hexa BDEs is much lower than that in North America (Park, et al. 2011), a 1 month-old infant in the UK is still more exposed to Σtri-hexa BDEs than in several other European countries via breast milk (Roosens, et al. 2010). Interestingly, the average exposure of a nursing infant to Σtri-hexa BDEs via breast milk exceeded upper-bound dietary intakes of UK adults and toddlers (UK Food Standards Agency 2006) (Figure 1), while for BDE-209, dietary exposure was the most significant exposure pathway for toddlers.

The low concentrations of BDE-209 in the studied milk samples resulted in much lower exposure of UK nursing infants to this contaminant than the USEPA reference daily dose (RfD) of 7 µg kg bw^{-1} day^{-1}. Similarly, our estimated UK infant daily intakes (Table 3) are lower than the USEPA reference doses for BDE-47 (100 ng kg bw^{-1} day^{-1} for neurodevelopmental toxicity) and Σtri-hexa BDEs (2000 ng kg bw^{-1} day^{-1} for liver toxicity) (U.S.EPA 2008). However, the median level of Σtri-hexa BDEs in this study (4.98 ng kg^{-1} lw) is slightly higher than that associated with congenital cryptorchidism (4.16 ng kg^{-1} lw; $p<0.01$) in Danish-Finnish newborn boys (Crump, et al. 2010) and generally in line with levels associated with irregular menstruation periods in a Taiwanese population (Chao, et al. 2010). While this does not provide solid evidence on the potential health effects associated with the reported levels of PBDEs in human milk due to the lack of relevant studies in the

285 UK, our results certainly raise concerns about potential adverse effects resulting from
286 exposure of infants and mothers to PBDEs. Although breastfeeding mothers should be
287 encouraged and supported due to the well-documented beneficial effects of breast feeding,
288 scientific studies ought to characterize and measure the contaminants in breast milk so that
289 protective measures may be provided, if necessary, to avoid any potential harmful effects on
290 the mother or the newborn.
291
292 *Comparison of PBDEs intake to human body burdens*
293 To convert daily adult intakes of BFRs via different exposure pathways to expected body
294 burdens, the bioaccessible fractions of each target compound (Abdallah, et al. 2012) were
295 used in equation 3 to substitute for AF_{PBDE} in case of exposure via dust ingestion or diet,
296 while the inhalable fraction was assumed to be 100% bioavailable. The body lipid mass was
297 estimated based on a 25% body fat for an average adult weighing 70 kg (U.S. EPA 1997).
298 Finally, K_{PBDE} was calculated as $0.693/t_{0.5}$; where $t_{0.5}$ is the half-life of the studied BFR in the
299 body lipid compartment (Geyer, et al. 2004).
300 In general, good agreement was observed between the predicted and the observed body
301 burdens of main target PBDEs (table 4) given the simplicity of the model used (e.g. only one
302 body compartment was studied), the dearth of information regarding the half-lives of
303 different PBDE congeners in various compartments of the human body, and the uncertainty
304 about the bioavailability of the studied compounds from different exposure routes.
305 In addition, the PK model used here does not estimate human exposure via routes such as
306 dermal contact and water intake. This is due to the high uncertainty and complete absence of
307 experimental data on the extent of BFR absorption via dermal contact by humans coupled
308 with the expected minimal contribution of water intake to the overall daily exposure to BFRs
309 based on the very low aqueous solubility of PBDEs.

Nevertheless, the good agreement between the predicted and observed results indicates that the studied exposure routes are the main pathways driving UK adult body burdens of PBDEs. This is in line with the findings of Lorber (Lorber 2008) who studied the exposure of Americans to PBDEs and reported indoor dust ingestion as the main route of exposure followed by diet and inhalation. However, more research is required for assessment of the bioavailability of various PBDEs via different exposure routes and determination of $t_{0.5}$ of PBDEs in various human tissues.

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Supplementary data

Specific details of analytical methodology, exposure estimation, QA/QC measurements and concentrations of target BFRs in each sample are available as supplementary data.

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Tables

Table1: Statistical summary of PBDE concentrations (ng g^{-1} lw) in human milk samples (n=35) from Birmingham, UK.

	BDE-47	BDE-49	BDE-85	BDE-99	BDE-100	BDE-153	BDE-154	∑tri-hexa	BDE-209
Average	3.30	<0.05	0.08	0.71	0.45	1.10	0.30	5.95	0.31
SD*	3.25	0.08	0.15	0.67	0.39	1.05	0.30	5.35	0.30
Median	2.80	<0.05	<0.05	0.69	0.38	0.91	0.21	5.00	0.25
DF (%)**	100	20	46	94	89	97	77	100	69
LOQ	0.043	0.045	0.051	0.055	0.053	0.058	0.059	N/A[#]	0.062
Minimum	0.17	<0.05	<0.05	<0.06	<0.05	<0.06	<0.06	0.2	<0.06
25^{th} %ile	0.78	<0.05	<0.05	0.20	0.12	0.35	0.07	1.70	<0.06
75^{th} %ile	5.15	<0.05	0.09	0.85	0.70	1.43	0.55	9.55	0.58
Maximum	14.65	0.45	0.83	3.43	1.86	4.57	11.10	26.10	0.92

* Standard deviation.

** Detection frequency.

[#] Not applicable.

552 **Table 2: Average concentrations of PBDEs (ng g^{-1} lw) in human milk samples from**
553 **different countries.**

Location	year	number	∑tri-hexa BDEs	BDE-209	Reference
UK	2009-10	35	5.9	0.3	(this study)
UK	2001-03	54	6.3	N/A*	(Kalantzi, et al. 2004)
Norway	2003-09	393	2.7	0.6	(Thomsen, et al. 2010)
Sweden	1996-2006	276	3.4	N/A	(Lignell, et al. 2011)
France	2004-06	93	2.5	1.6	(Antignac, et al. 2009)
Spain	2005	9	2.1	2.5	(Gomara, et al. 2011)
Belgium	2006	22	3.0	5.9	(Roosens, et al. 2010)
Italy	2005-07	13	1.3	N/A	(Alivernini, et al. 2011)
USA	2002	47	34.0	0.9	(Schecter, et al. 2003)
Canada	2003	10	50.4	0.4	(She, et al. 2007)
Australia	2007	10	7.6	0.3	(Toms, et al. 2009)
China	2004	19	2.5	3.0	(Sudaryanto, et al. 2008)
India	2009	45	1.1	0.4	(Devanathan, et al. 2012)
Korea	2008-09	21	2.7	N/A	(Kim, et al. 2011)
Tunisia	2010	36	8.3	N/A	(Ben Hassine, et al. 2012)

554 * N/A not analyzed

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562 **Table 3: Estimated exposure* (ng (kg bw)$^{-1}$ day^{-1}) of a 1 month old infant to the target**
563 **BFRs via breast milk under different scenarios**.**

	25th %ile	Average	Median	75th %ile
BDE-47	4.6	19.3	16.3	30.3
BDE-99	1.2	4.2	4.0	5.1
BDE-100	0.7	2.7	2.2	4.2
BDE-153	2.1	6.5	5.3	8.4
BDE-154	0.4	1.7	1.3	3.2
Σtri-hexa BDEs	10.0	34.9	29.4	56.4
BDE-209	<0.1	1.8	1.2	3.4

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565 * Values below LOQ were assumed to be 1/2 LOQ.

566 ** Based on an average body weight of 4.14 kg and a daily lipid intake of 24.4 g lipid day^{-1}

567 (U.S. EPA 2002.).

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575 **Table 4: Comparison of predicted adult body burdens arising from average and median**
576 **daily exposures[#] to major target PBDEs with observed levels in human milk samples.**

	BDE-47	BDE-99	BDE-100	BDE-153	BDE-154	Σ_5BDEs	BDE-209
Average intake* (ng day^{-1})							
Dust[a]	1.10	1.80	0.24	0.31	0.17	3.70	4270
Diet[b]	35	30	5.60	7.00	2.80	80	310
Air[c]	0.90	0.60	0.14	0.05	0.03	1.70	9.40
Median intake* (ng day^{-1})							
Dust[a]	0.29	0.67	0.08	0.12	0.01	1.20	2975
Diet[b]	35	30	5.60	7.00	2.80	80	310
Air[c]	0.20	0.30	0.04	0.01	0.01	0.55	7.40
Average predicted body burdens (ng g^{-1} lw)							
Dust	0.06	0.05	0.01	0.02	0.01	0.14	0.34
Diet	3.33	1.39	0.38	1.15	0.16	6.40	0.03
Air	0.11	0.05	0.01	0.01	0.01	0.20	0.01
Sum	3.49	1.49	0.40	1.19	0.18	6.74	0.38
Median predicted body burdens (ng g^{-1} lw)							
Dust	0.01	0.02	0.00	0.01	0.00	0.04	0.24
Diet	3.33	1.44	0.38	1.15	0.16	6.45	0.03
Air	0.03	0.03	0.00	0.00	0.00	0.06	0.00
Sum	3.36	1.48	0.39	1.16	0.16	6.55	0.27
Observed body burdens (ng g^{-1} lw)							
Average	3.28	0.71	0.45	1.09	0.28	5.92	0.31
Median	2.77	0.68	0.38	0.9	0.21	4.98	0.24

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578 [#] Values below LOQ were assumed to be 1/2 LOQ.

579 * Based on average adult dust ingestion rate of 20 mg day^{-1} (Jones-Otazo, et al. 2005),
580 average inhalation rate of 20 m^3 day^{-1} (Currado and Harrad 1998) and average adult weight
581 of 70 kg.

582 [a] Estimated from reference (Harrad, et al. 2008a); [b] Estimated from reference (UK Food
583 Standards Agency 2006); [c] Estimated from references (Harrad, et al. 2006; Stapleton, et al.
584 2009).

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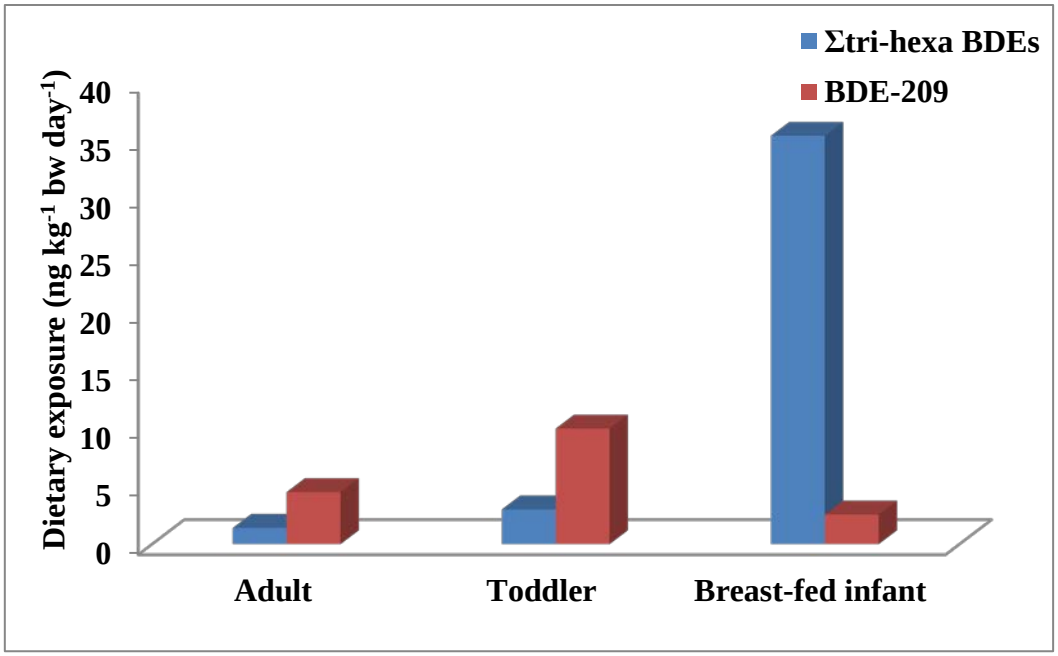
589 **Figure 1: Average estimates of dietary exposure (ng (kg bw)$^{-1}$ day^{-1}) of UK adults*,**

590 **toddlers* and breast-fed infants** to PBDEs.**



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592 * From reference (UK Food Standards Agency 2006); ** This study.

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